From Genetic Risk Awareness to Overt Type 1 Diabetes

Parental stress in a placebo-controlled prevention trial

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OBJECTIVE — To evaluate the psychological burden of parents facing increasing risk of type 1 diabetes in their children.

RESEARCH DESIGN AND METHODS — In the population-based Type 1 Diabetes Prediction and Prevention (DIPP) Study, newborn infants with HLA-DQB1–conferred diabetes risk were enrolled in sequential analyses of diabetes-associated autoantibodies. Those persistently positive for at least two autoantibodies were recruited to a randomized double-blinded intervention trial. The experience of stress in parents of 664 children was measured using Parenting Stress Index self-report inventory.

RESULTS — While diagnosis of diabetes increased parental stress, the appearance of autoantibodies or participation in the intervention trial did not. Mothers had higher stress levels than fathers. Single parenthood and chronically ill family members increased parental stress.

CONCLUSIONS — Parental stress was not increased by notification of autoantibody positivity or by participation in an intervention trial. Other demanding family conditions contributed to the experience of stress.

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Natural history and prevention studies screening genetic risk for type 1 diabetes have raised concerns of the burden of risk awareness in asymptomatic individuals, most of whom will never develop the disease (1,2).

RESEARCH DESIGN AND METHODS

Study subjects

The population-based Type 1 Diabetes Prediction and Prevention (DIPP) Study screened neonates for HLA-DQB1–conferred diabetes risk, enrolling children at risk in sequential monitoring for diabetes-associated autoantibodies. Children permanently positive for multiple autoantibodies were invited to a randomized double-blinded prevention trial comparing intranasal insulin with placebo (3).

Parents of 1,125 participants received a self-administered questionnaire (see below). There were 1,204 questionnaires (59%) returned by parents of 664 children. A total of 457 children showed genetic predisposition only, whereas 188 had diabetes-associated autoantibodies and 19 had progressed to diabetes. The time from notification of autoantibody positivity ranged from 0.5 to 6.7 years (mean 2.9).

A total of 35 parents had a child diagnosed with diabetes, and 326 had a child with diabetes-associated autoantibodies only. There were 18 parents of a child with diabetes (51.4%) and 84 parents of an autoantibody-positive child (25.8%) who enrolled their child in the prevention trial. There were 69 parents who had a child eligible for the trial but had chosen not to participate, whereas the children of 173 parents had tested only transiently positive for one autoantibody species. A total of 843 control parents, whose child had not developed autoantibodies, were matched with the parents of children with diabetes ($n = 197$) or autoantibodies ($n = 646$) for parental age, child's age, and study site. Age, employment, marital status, place of living, and chronic illness in the family were recorded.

Measurement of parenting stress

Eleven questions focusing on parenting stress were selected from the 34-item Swedish version (4) of the Parenting Stress Index self-report inventory (5) and modified to this scale with a four-factor construction. An index describing "parental stress" was calculated from the mean of the scores. Four additional factors (relationship with spouse, sense of competence of parenthood, social life, and privacy) were assessed (scale 1–7 from worst to best).

Statistical analyses

Scores were compared using independent samples' t test. The associations between parental stress, time from notification of the autoantibody result, and duration of the study were examined using linear regression analysis. Association between group and categorical variables in the epidemiological data were tested with χ^2 statistics. The effect of epidemiological variables was analyzed with regression

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Table 1—*Parental stress expressed as parental stress index, with lower scores indicating higher stress levels*

Parental stress index							
Parents of an autoantibody-positive child				Parents of a child with diabetes			
	Mean	SEM	*P*		Mean	SEM	*P*
Autoantibody-positive child	4.50	0.05		Child with diabetes	4.18	0.12	0.005
Control	4.52	0.03		Control	4.56	0.05	
Mothers	4.64	0.07	0.005	Mothers	4.09	0.07	
Fathers	4.38	0.06		Fathers	4.29	0.06	
Transient autoantibodies	4.50	0.06					
Multiple permanent	4.49	0.07					
Participated in intervention	4.48	0.10		Participated in intervention	4.16		
Eligible, did not participate	4.51	0.11		Eligible, did not participate	4.21		
Living alone	3.95	0.18	0.001	Living alone	3.25	0.43	0.012
Living as couples	4.55	0.05		Living as couples	4.27	0.11	
Chronic illness in family	4.26	0.11	0.001	Chronic illness in family	3.73	0.29	0.03
No chronic illness	4.58	0.05		No chronic illness	4.32	0.11	
Unemployment	4.45	0.13		Unemployment	3.97	0.37	
No unemployment	4.61	0.06		No unemployment	4.68	0.10	
Urban environment	4.42	0.06	0.027	Urban environment	4.09	0.15	
Rural environment	4.64	0.05		Rural environment	4.34	0.21	

P values are given for statistically significant differences.

and univariate ANOVA. The SPSS for Windows release 11.0 software (SPSS, Chicago, IL) was used.

RESULTS

Sociodemographic characteristics

The parent groups were closely similar. Most lived in couples; however, more parents in the autoantibody-positive group than the control group lived alone (7.7 vs. 4.2%, $P = 0.03$). The proportion of chronically ill adults was higher in the autoantibody-positive group than in the control group (23.9 vs. 16.5%, $P = 0.007$); also, the unemployment rate tended to be higher. Similar trends were seen in the diabetic group.

Parenting stress

Stress indexes were similar in parents of antibody-positive children and control parents. Fathers experienced less stress than mothers (Table 1), considered parenthood easier ($P = 0.008$), and had more time for private life than mothers ($P < 0.0001$; data not shown). Control parents showed similar sex difference. Transient autoantibody positivity or the presence of multiple permanent autoantibodies in the child did not alter parental stress level. Of note, parental stress was similar whether or not the child participated in the prevention trial. There was no difference between parents of trial participants and parents who chose not to enroll an eligible child (Table 1).

Parents whose child had developed diabetes showed higher stress than control subjects (Table 1). They also considered child care and parenthood more difficult ($P = 0.032$; data not shown) and regarded parents' responsibilities more demanding and social relations more difficult. They had more marital problems and more distant relation with their spouse than the control subjects ($P = 0.013$). The answers of the mothers and fathers were similar.

Parental stress decreased with duration of the follow-up ($r = 0.142$, $P = 0.01$). Single parents had higher stress than couples. Urban environment, unemployment, and chronic illness in the family were associated with higher stress. Parental stress increased with maternal age ($r = -0.115$, $P = 0.039$) but not with paternal age.

CONCLUSIONS — Parental stress was not increased when the family learned that their child had progressed to autoantibody positivity, or during the prevention trial. At enrollment, the implication was that although the 2–8% genetic risk was greater than the 0.7% in the background population, the odds were still strongly against a particular child to develop diabetes. Multiple autoantibodies increased the risk to >50%. The prevention trial presented a choice of taking an action with potentially beneficial consequences, or leaving the child without this option. The urge to do something to prevent diabetes is strong (6), and parents may see an intervention trial either as an opportunity to actively interfere in the course of events, or a daily reminder of the risk.

Parental anxiety is not significantly elevated in screening programs for type 1 diabetes risk and further dissipates over time (7–10). We did not observe the temporary increase in anxiety after notification of positive autoantibody results reported in some other studies (11). In agreement with the experiences in the Diabetes Prevention Trial–Type 1 (DPT-1) Study (11,12), even the long-term randomized prevention trial did not increase parental stress. In the ethnically homogeneous and well-educated Finnish population, the problems involved are probably smaller than in many other countries.

Mothers had higher stress than fathers, regarded parenthood as more demanding, and needed more social support. This may reflect traditional pa-

rental roles or a differential effect of risk awareness. Unrelated life experiences like single parenthood and chronic illness in the family increased the stress and may call for special attention.

Stress and early negative life events may associate with increased risk of chronic diseases, including type 1 diabetes (13–15). The association between the development of autoimmunity and potentially stressful life circumstances (Table 1) supports this theory.

In conclusion, in a large population-based cohort of children at increased genetic risk for type 1 diabetes, parental stress was not increased by notification of autoantibody positivity or participation in the double-blinded prevention trial. The burden of risk awareness can be minimized by proper study setup.

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